

REMARKS/ARGUMENTS

Claims 1, 2, and 4-30 were pending in this application, of which claims 1, 2, 4-9, 11, 15-18, and 29-30 were under consideration.

Applicants submit herewith a substitute specification that substantially conforms to the preferred format outlined by the Examiner. It is respectfully submitted that no new matter has been added. Entry of the substitute specification is respectfully requested.

Claims 1, 6-14, 16-20, and 22-28 have been amended. Claims 2, and 4-5 have been canceled. Support for the amendments may be found throughout the original specification and claims. As such, it is submitted that no new matters enters by way of the present amendment.

Claims 10, 12-14, and 19-28 have been withdrawn from consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected inventions or species, pending rejoinder upon allowance of linking product and generic claims. Hence, claims 1 and 6-30 remain pending, of which claims 1, 6-9, 11, 15-18, and 29-30 are under consideration. Entry of the amendment and reconsideration of the subject application as amended is respectfully requested.

Election/Restriction

The finality of the election/restriction requirement is acknowledged, pending rejoinder upon allowance of linking product and generic claims.

Objection to the Specification

The Specification has been objected to as allegedly not complying with the preferred layout of a utility application. Further to the Examiner's request, a Substitute Specification is submitted herewith substantially complying with the applicable specification sections of the preferred layout. As such, withdrawal of this objection is respectfully requested.

Claim Objections

Claims 1-2, 4-8, and 16-17 are objected to due to the alleged typographical error "characterised." To expedite prosecution, Applicants have incorporated the Examiner's

suggestion and amended the claims to recite "characterized". However, such amendments do not narrow the scope of the claims in any regard.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

Claim 1 stands rejected under 35 U.S.C. §112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In part, claim 1 is indefinite because it is allegedly unclear whether the "cell-bound or soluble molecule" applies to the reagent or to the target. While not agreeing that the claim is indefinite in this regard, in order to expedite prosecution, claim 1 has been amended to recite a cell-bound or soluble target molecule. However, such amendment does not narrow the scope of the claim.

Further, claim 1 is allegedly indefinite due to the recitation of the term "latter". Again, in order to expedite prosecution, the claim has been amended to recite interaction with the cell-bound or soluble target molecule. However, such amendment does not narrow the scope of the claim.

As such, it is submitted that the claims comply with 35 U.S.C. §112, second paragraph, and withdrawal of this rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. § 112, first paragraph - Written Description

Claims 1-2, 4, 6, 8, 9, 11, 15-16 and 29-30 stand rejected under 37 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

The Examiner acknowledges that the written description sets forth an antibody binding to a core domain, CEPDY, of CD30 protein, but alleges that the claims do not limit any particular conserved structural attributes for the reagent.

While not agreeing that the claims lack adequate written description in the specification, independent claim 1 has been amended to recite that the cell-bound or soluble target molecule is CD30, and that the reagent binds to an epitope with a core sequence CEPDY. As such, the claims provide a particular conserved structural attribute for the reagent, i.e., a specific epitope binding domain. Further, the claims are limited to reagents selected from

antibodies, antibody fragments, chimerized antibodies, humanised antibodies, single chain (sc)Fv fragments, scT-cell receptor (TCR) fragments, and hybrid scFv/scTCR fragments. As such, contrary to the statement in the Office Action regarding the scope of the term “reagent”, all of the claimed reagents are compounds comprising a protein structure capable of binding to an epitope with a core sequence CEPDY.

The claimed structural attribute of the core sequence of the epitope to which the reagents bind provide “structural feature[s] possessed by members of the [claimed] genus that distinguish[] them from others.” *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). In contrast to the mere name “cDNA” provided in *Eli Lilly*, Applicants have provided a structural feature common to the genus. Such a common structural feature is not “a mere statement that it is part of the invention.” *Office Action mailed June 6, 2005* at Page 6. Accordingly, Applicants submit that one of ordinary skill in the art would have recognized that at the time of filing Applicants had possession of the claimed invention.

For at least these reasons, it is submitted that the claims comply with 35 U.S.C. §112, first paragraph, and withdrawal of this rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. § 112, first paragraph - Enablement

Claims 7, 15-18 stand rejected under 37 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement.

Cell DSZ1 stored at the German Microorganisms Collection (DSM) under the number DSM ACC2548, described, e.g., at page 9 of the specification, has been deposited at the German Microorganisms Collection (DSM) under accession number DSM ACC2548 in accordance with the Budapest Treaty. A declaration confirming the conditions of the deposit accompanies this response (Exhibit C).

As such, it is submitted that the claims comply with 35 U.S.C. §112, first paragraph, and withdrawal of this rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. § 102

A. Gravekamp

Claims 1-2 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by the cited portions of Infection and Immunity, Vol. 64, p. 3572-3583, September 1996, Gravekamp, *et al.* (hereinafter "Gravekamp"). This rejection is respectfully traversed for at least the reasons which follow.

The rejected claims generally relate to a reagent that enters into interactions with at least two spatially separated positions on a cell-bound or soluble target molecule; wherein the cell-bound or soluble target molecule is CD30; the at least two spatially separated positions each comprise an epitope having a core sequence CEPDY; and the reagent enters into interactions with each of the at least two spatially separated positions on the cell-bound or soluble target molecule via binding to the epitope with a core sequence CEPDY.

It is well established that to anticipate a claim, a reference must disclose every element of the claim. *Verdegaal Bros. v. Union Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 U.S.P.Q.2d 1913 (Fed. Cir. 1989).

Whatever else Gravekamp does disclose, it does not, at a minimum, disclose a reagent capable of interacting with a target molecule, wherein the target molecule is CD30. Absent such a teaching, Gravekamp does not anticipate the present claims. As such, for at least this reason, withdrawal of this rejection is respectfully requested.

B. Lemke

Claims 1-2, 4-6, 15 and 29-30 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by the cited portions of U.S. Patent No. 6,033,876 to Lemke, *et al.* (hereinafter "Lemke").

Again, the rejected claims generally relate to a reagent that enters into interactions with at least two spatially separated positions on a cell-bound or soluble target molecule; wherein the cell-bound or soluble target molecule is CD30; the at least two spatially separated positions each comprise an epitope having a core sequence CEPDY; and the reagent enters into

interactions with each of the at least two spatially separated positions on the cell-bound or soluble target molecule via binding to the epitope with a core sequence CEPDY.

Whatever else Lemke does disclose, it does not disclose a reagent that interacts with at least two spatially separated positions on CD30, or a reagent which binds an epitope with a core sequence CEPDY.

In support of the rejection, the Examiner acknowledges that Lemke does not specifically disclose that the antibodies bind to two spatially separated positions on cell-bound or soluble CD30. However, the Examiner asserts that “[i]n the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed produce is different from those taught by the prior art and to establish patentable differences.” *Office Action mailed June 6, 2005* at Page 10.

The cases cited by the Examiner do not support shifting the burden to the applicant unless the Examiner has first established that the claims are “*reasonably* considered as possessing the allegedly inherent characteristics” of the prior art (*In re Best*, 195 USPQ 430, 433 (CCPA 1977), emphasis added). “Inherency ... may not be established by *probabilities or possibilities*.” *Mehl/Biophile v. Milgraum*, 52 USPQ2d 1303, 1305 (Fed. Cir. 1999) (emphasis added). “The mere fact that a certain thing *may* result from a given set of circumstances is *not sufficient* to establish inherency.” *In re Rijckaert*, 28 USPQ2d 1955 (Fed. Cir. 1993) (emphasis added).

Even when antibodies are elicited in one strain of inbred mice against a small haptenic antigen such as azophenylarsonate (MW 217), the resulting antibodies have different sequences and different binding characteristics. See Capra *et al.*, *Immunology Today* 3:332-339 (1982). If antibodies are elicited in different subjects against a much larger and structurally much more complex antigen such as the CD30 (MW 120,000), the diversity of properties is expected to be even greater. Here, Lemke does little more than establish the existence of various anti-CD30 binding molecules. In fact, Lemke itself establishes the variability of binding characteristics of anti-CD30 binding molecules (*see, e.g., Lemke*, Col. 13, line 62 - Col. 14, line 12 and Table II). Given the great variability in antibodies elicited to a single target, it would be mere coincidence if the antibody of Lemke happened by chance to interact with two spatially

separated positions on CD30, as well as bind to the core sequence CEPDY, as required by the independent claim.

As discussed above, inherency cannot be based on probabilities or possibilities, particularly such remote ones. Therefore, it is submitted that the Examiner has not established a *prima facie* case of inherency to require rebuttal evidence from applicants. For at least these reasons, this rejection is respectfully traversed, and withdrawal of this rejection is respectfully requested.

C. Mohler

Claims 1 and 5 stand rejected under 35 U.S.C. §102(e) as being allegedly anticipated by the cited portions of U.S. Patent Publication No. 2002/0064527 to Mohler, *et al.* (hereinafter "Mohler"). This rejection is respectfully traversed for at least the reasons which follow.

Whatever else Mohler does disclose, it does not disclose a reagent that interacts with at least two spatially separated positions on CD30, or a reagent which binds an epitope with a core sequence CEPDY.

In support of the rejection, the Examiner states that Mohler discloses polyclonal antibodies against "CD30 antigenic polypeptides," but alleges that "it would be reasonable to conclude that the antibodies include the antibody, which specifically bound to the core sequence CEPDY of CD30." *Office Action mailed June 6, 2005* at Page 11. Applicants respectfully traverse.

As discussed above, inherency cannot be based on probabilities or possibilities. Given the great variability in antibodies elicited to a single target, it would be mere coincidence if the antibody of Mohler happened by chance to interact with two spatially separated positions on CD30, as well as bind to the core sequence CEPDY, as required by the independent claim. Therefore, it is submitted that the Examiner has not established a *prima facie* case of inherency to require rebuttal evidence from applicants.

For at least these reasons and the reasons discussed above with reference to Lemke, this rejection is respectfully traversed, and withdrawal of this rejection is respectfully requested.

D. Francisco

Claims 1-5, 8-9 and 15-16 stand rejected under 37 U.S.C. §102(e) as being allegedly anticipated by the cited portions of U.S. Patent Publication No. 2004/0018194 to Francisco, *et al.* (hereinafter "Francisco"). This rejection is respectfully traversed for at least the reasons which follow.

Whatever else Francisco does disclose, it does not disclose a reagent that interacts with at least two spatially separated positions on CD30, or a reagent which binds an epitope with a core sequence CEPDY.

The Examiner states that Francisco discloses anti-CD30 antibodies. In support of the rejection, the Examiner acknowledges that Francisco does not specifically disclose that the antibodies bind to two spatially separated positions on cell-bound or soluble CD30. However, the Examiner asserts that "[i]n the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed produce is different from those taught by the prior art and to establish patentable differences." *Office Action mailed June 6, 2005* at Page 11-12. Applicants respectfully traverse.

As discussed above, inherency cannot be based on probabilities or possibilities. Given the great variability in antibodies elicited to a single target, it would be mere coincidence if the antibody of Francisco happened by chance to interact with two spatially separated positions on CD30, as well as bind to the core sequence CEPDY, as required by the independent claim. Therefore, it is submitted that the Examiner has not established a *prima facie* case of inherency to require rebuttal evidence from applicants.

For at least these reasons and the reasons discussed above with reference to Lemke, this rejection is respectfully traversed, and withdrawal of this rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 1, 8-9 and 11 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Lemke, in view of the cited portions of Deonarain, *et al.*, *Br. J. Cancer*, Vol. 70, p. 786-94 (1994) (hereinafter "Deonarian"). This rejection is respectfully traversed for at least the reasons which follow.

As discussed above, whatever else Lemke does disclose, it does not disclose a reagent that interacts with at least two spatially separated positions on CD30, or a reagent which binds an epitope with a core sequence CEPDY. Given the great variability in antibodies elicited to a single target, it would be mere coincidence if the antibody of Lemke happened by chance to interact with two spatially separated positions on CD30, as well as bind to the core sequence CEPDY, as required by the independent claim.

Without agreeing that one of skill in the art would be motivated to combine the teaching of Deonarian and Lemke, even assuming *arguendo* such a combination, Deonarian does nothing to remedy the deficiencies of Lemke.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination must be found in the prior art, and not be based on applicants' disclosure. *See M.P.E.P.* §§2143.01 and 2143.03.

Absent a teaching or suggestion, either in the references themselves or the knowledge of those skilled in the art, to modify the antibodies of Lemke to arrive at the presently claimed reagents, it is submitted that the cited references do not render the claimed invention obvious.

The patentability of the presently claimed invention, as compared to the state of the art, is further evidenced by the unexpected ability of the claimed reagent to bind to at least two spatially separate positions on the target molecule. Due to this ability, the claimed reagent possesses a much higher probability that the target molecule does not completely lose its ability to be recognized by the reagent in case a mutation occurs in the target molecule. In contrast, with

binding compounds known from the state of the art, there is a high risk of this to happen. For example, if the mutation affects the binding site on the target molecule, either directly (*e.g.*, within the epitope) or indirectly (*e.g.*, by a conformation change), this leads to a loss of the ability of the binding molecule to recognize the target site (*see, e.g.*, page 2, second paragraph of the original specification). As a result, *e.g.*, in the context of diagnostics, an incorrect negative result would be produced and subsequent therapy could fail completely. Because the presently claimed reagent enters into interaction with the target molecule in at least two positions, the loss of one of the binding sites, *e.g.*, by mutation, does not lead to complete loss of the binding since the reagent still reacts with a second binding site. This surprising property of the presently claimed invention results, *inter alia*, in a clearly increased reliability of diagnosis.

In addition, the presently claimed reagent surprisingly also produces an increased sensitivity in diagnosis and an increased effectiveness in therapy (*see, e.g.*, page 3, third paragraph of the original specification). The increased sensitivity stems, in part, from the fact that twice as much reagent can bind to a single cell compared to reagents known in the art. The increased amount of binding of the reagent in turn leads to a stronger detection signal of the sample to be analyzed. In the context of therapy, this surprising property is also very versatile since compared to binding molecules known in the art, due to a stronger binding to the target molecule, a larger quantity of reagent can be taken up by a target cell so that a correspondingly stronger therapeutic effect on the target cell may be elicited, *e.g.*, by activation of the complementary system or by incorporation of toxins or radioactive isotopes which can ultimately kill the target cell (*see, e.g.*, page 3, third paragraph of the original specification) resulting in a more effective therapy.

Finally, the particular surprising properties of a reagent encompassed by the amended claims have also been demonstrated in the Examples of the specification. Such reagents bind CD30 with high affinity (*see, e.g.*, page 15, second paragraph of the original specification), and are able to produce a strong antibody-dependent cytotoxicity (*see, e.g.*, page 15, last paragraph to page 16, first paragraph of the original specification).

Regardless of the unexpected properties of the claimed reagents, it is submitted that the Examiner has failed to establish a *prima facie* case of obviousness. Whatever else

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Lemke and Deonarain may disclose or suggest, neither reference alone or in combination suggests the desirability of a reagent capable of interacting with two spatially separated positions on CD30, as well as binding to the core sequence CEPDY. For at least these reasons, this rejection is traversed, and withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,



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